REMARKS

Claims 1, 4-28, 43-45, and 76-77 are currently pending in the above-identified application. Claims 2-3, 29-42, 46-75, and 78-141 have been cancelled by this amendment. Claims 142-163 are added by this amendment. Accordingly, claims 1, 4-28, 43-45, 76-77, and 142-163 remain for consideration in the above-identified patent application.

Claims 29-41, 46-75, and 78-141 were withdrawn from prosecution pursuant to 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention. The species "adenovirus" is elected for prosecution and claim 23 is amended to reflect that election.

Please note that on the Office Action Summary, claims 24, 25, and 29-141 were listed as being withdrawn from consideration. This listing in the Office Action Summary appears to be erroneous in view of the discussion in the Office Action. Clarification is requested. The listing above is based on the discussion in the Office Action.

Claims 1-23, 26-28, 43-45, and 76-77 were rejected under the second paragraph of 35 U.S.C. § 112 for alleged indefiniteness.

Claims 1-10, 12-23, 26-28, 42-45, and 76-77 were rejected under the first paragraph of 35 U.S.C. § 112 for alleged failure to comply with the written description requirement.

Claims 1-10, 12-23, 26-28, 42-45, and 76-77 were also rejected under the first paragraph of 35 U.S.C. § 112 for alleged failure to comply with the enablement requirement.

Claims 1-3, 5-23, and 26-28 were rejected under 35 U.S.C. § 102(b) as anticipated by PCT Patent Publication No. WO 00/00506 by Kato et al. ("Kato et al. '506").

Reexamination of the application as amended, reconsideration of the rejections, and allowance of the claims remaining for consideration are respectfully requested.

The three-month shortened statutory period for response expires on March 17, 2005. Accordingly, this response is being filed in a timely manner.

I. AMENDMENTS TO THE APPLICATION

Entry of the amendments to the application is respectfully requested. As detailed below, the amendments introduce no new matter.

The specification is amended to explicitly recite the sequence of EST Accession no. AA098865, which now becomes SEQ ID NO:37. Exhibit A, attached hereto, is a printout of the NCBI database entry for EST Accession No. AA098865, which shows that the entry for this nucleotide database accession number was created on October 28, 1996 and has not been updated since. Therefore, the sequence represented by EST Accession no. AA098865 has not changed, and that a reference to this EST Accession no. is unambiguous. Accordingly, Applicants are entitled to add this sequence to the specification, because one of ordinary skill in the art would know that this was the sequence referred to and that there is no other sequence to which the designation EST Accession no. AA098865 would be applicable. This is analogous to the addition of physical properties of compound such as optical rotation data, which are inherent properties of the compound and can be added to the disclosure after filing. Ex parte Davisson, 133 U.S.P.Q. 400 (Pat. Off. Bd. App. 1958). This is also analogous to adding

a structural formula for a compound that had been sufficiently identified as to its physical and chemical characteristics so that it could have been identified apart from the method by which it had been produced, which is also permissible when, as here, the identification would be unambiguous. Ex parte Fox, 128 U.S.P.Q. 157 (Pat. Off. Bd. App. 1957).

Other amendments to the specification are made only to correct obvious typographical and spelling errors: e.g., "nemotode" for nematode, "occular" for ocular, "manitol" for mannitol, and to correct a subscript that clearly was intended to have been a superscript. These corrections introduce no new matter.

The claims are amended to recite the sequence of EST Accession no. AA098865 explicitly with the sequence identifier SEQ ID NO:37 and to make other corrections to remove language considered indefinite by the Examiner in order to advance prosecution. The claims are also amended, where appropriate, to recite a greater than 91.6% identity between the sequence claimed and that of SEQ ID NO:1. This is supported at, e.g., page 3, lines 5-7 of the specification, where it is clearly stated that all nucleotide sequences having at least about 70% identity to SEQ ID NO:1 are part of the invention. Thus, sequences with greater than 91.6% identity to SEQ ID NO: 1 are clearly to be regarded as part of the invention. This is analogous to the cancellation of some members of a Markush group to leave fewer than the original number of members, which is permissible. In re Ruff, 118 U.S.P.Q. 340 (C.C.P.A. 1958).

This response is being filed in accordance with recently revised 37 C.F.R. § 1.121, as set forth in 68 F.R. 38611 (June 30, 2003). If the amendment is considered to be not in compliance with recently revised 37 C.F.R. § 1.121, the Examiner is respectfully requested to contact the undersigned at his earliest possible convenience.

Accordingly, entry of these amendments is respectfully requested.

II. THE REJECTIONS UNDER THE SECOND PARAGRAPH OF 35 U.S.C. § 112

Claims 1-23, 26-28, 43-45, and 76-77 were rejected under the second paragraph of 35 U.S.C. § 112 for alleged indefiniteness. The various grounds for indefiniteness are dealt with below as cited by the Examiner. It is believed that amendments made to these claims have obviated any basis for indefiniteness, and the Examiner is therefore respectfully requested to withdraw these rejections. To the extent that the amendments to the claims are not considered to have obviated any of these bases for rejection, they are respectfully traversed.

A. The Rejection for the Recitation of "At Least About" in Claims 1-4, 17, 43-45, and 76

The term "at least about" in claims 1-4, 17, 43-45, and 76 was stated to be relative and thus indefinite. Claims 11-15, 18-23, 26-28, and 77 were also considered to be indefinite because they are dependent claims that encompass all of the limitations of the independent claim. This rejection is obviated by the deletion of the word "about" in this phrase, and the Examiner is therefore respectfully requested to withdraw this rejection.

B. The Rejection for the Recitation of the Term "Less Than About" in Claims 5-9

The term "less than about" in claims 5-9 was stated to be relative and thus indefinite. The word "about" was deleted from this phrase by amendment, and this is believed to obviate this basis for rejection. The Examiner is therefore respectfully requested to withdraw this rejection.

C. The Rejection for the Recitation of the Term "Less Than About" in Claim 10

The term "less than about" in claim 10 was also stated to be relative and to render that claim indefinite. The word "about" was deleted from this phrase by amendment, and this is believed to obviate this basis for rejection. The Examiner is therefore respectfully requested to withdraw this rejection.

D. The Rejection for the Recitation of the Term "a Length of About" in Claim 16

The term "a length of about" in claim 16 was also stated to be relative and to render that claim indefinite.. The word "about" was deleted from this phrase by amendment, and this is believed to obviate this basis for rejection. The Examiner is therefore respectfully requested to withdraw this rejection.

E. The Rejection of Claim 10 for Failing to Claim the Base Size Ranges in the Alternative

Claim 10 was also rejected as indefinite under the second paragraph of 35 U.S.C. § 112 for failing to recite the base size ranges in the alternative. It was stated that it was unclear how a sequence can be "between about 2.5kB and 1kB, 1kB and 0.5kB, 0.5kB and 0.25kB and 0.1kB and 15 base pairs." This claim has now been amended to merely recite that the sequence is between 2.5 kB and 15 base pairs, the total range of base pair sizes encompassed by these alternatives. There is no ambiguity in this recitation. The Examiner is therefore respectfully requested to withdraw this basis for rejection.

F. The Rejection of Claim 13 for Lack of Clarity in Recitation of a Plurality of Sequences

Claim 13 was also rejected under the second paragraph of 35 U.S.C. § 112 as indefinite. It was stated that claim 13 included the phrase "wherein the sequence comprises a plurality of sequences attached to a substrate." The Examiner stated it was unclear how one sequence could comprise a plurality of sequences. This claim has now been amended to clarify that what is being claimed is a composition comprising a plurality of sequences, each of claim 1, attached to a substrate. This amendment removes any basis for rejection for indefiniteness of this claim on these grounds. The Examiner is therefore respectfully requested to withdraw this rejection.

G. The Rejection of Claims 1-16 and 26-28 for Failure to Recite the Sequence of the EST Used for Comparison

Claims 1-16 and 26-28 were rejected under the second paragraph of 35 U.S.C. § 112 for indefiniteness. It was stated that the limitation "wherein the sequence is distinct from EST Accession no. AA098865" made these claims indefinite because there was no recitation of the sequence of EST Accession no. AA098865 in the specification or claims. In order to correct this, the specification and claims have been amended to recite the explicit sequence of this nucleic acid segment, as explained above in Section (I) of these Remarks. Accordingly, the Examiner is therefore respectfully requested to withdraw this basis for rejection.

III. THE REJECTIONS UNDER THE FIRST PARAGRAPH OF 35 U.S.C. § 112

A. The Rejections of Claims 1-10, 12-23, 26-28, 42-45, and 76-77 Under the First Paragraph of 35 U.S.C. § 112 for Failure to Comply with the Written Description Requirement

Claims 1-10, 12-23, 26-28, 42-45, and 76-77 were rejected under the first paragraph of 35 U.S.C. § 112 for lack of compliance with the written description requirement.

As applied to the amended claims, this rejection is respectfully traversed. The basic test under the written description requirement of 35 U.S.C. § 112 is well established. All that is required to satisfy the written description requirement of the first paragraph of 35 U.S.C. § 112 is that the patent specification describes the claimed invention in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed subject matter, to ensure, e.g., that the invention had possession of the claimed subject matter as of the desired priority date. Regents of the University of California v. Eli Lilly & Co., 43 U.S.P.Q. 2d 1398 (Fed. Cir. 1997). In the context of nucleic acids, the recitation of structure for the claimed subject matter need not be great in order to satisfy the written description requirement. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of a genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Regents of the University of California, 43 U.S.P.Q. 2d at 1406. Moreover, it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in the application by "other appropriate language." Id.

This basic standard for compliance with the written description requirement under the first paragraph of 35 U.S.C. § 112 is satisfied by recitation of the required degree of identity in the claims. Identity of a nucleic acid sequence is a strict standard; either two bases in a sequence are identical, when the sequences are properly aligned, or they are not identical. Therefore, the percentage of identity recited in these claims provides sufficient relevant identifying characteristics to meet this standard.

The "Guidelines for Examination of Patent Examinations Under the 35 USC § 112 para. 1 'Written Description' Requirement," 66 Fed. Reg. 1099 (January 5, 2001) issued by the United States Patent and Trademark Office, state that the policy goals of the written description requirement are to: (i) clearly convey to the public what was invented; (ii) put the public in possession of what the applicant claims as the invention; and (iii) prevent an applicant from claiming subject matter that was not described in the specification as filed. These policy requirements are met by the amended claims.

Moreover, possession of the claimed invention can be shown by any of: (1) actual reduction to practice; (2) a "clear depiction" of the invention in detailed drawings; or (3) a description of sufficient relevant identifying characteristics. These requirements are met. There is actual reduction to practice in terms of the recitation of SEQ ID NO:1 and the protein encoded by this sequence, SEQ ID NO:2.

It is not the purpose or rationale of the written description requirement to define the function of claimed nucleic acid sequences. Once sufficient identifying characteristics are provided to enable one of ordinary skill in the art to conclude that the inventors had possession of the invention, the written description requirement has been satisfied. The nucleic acid sequences recited meet the requirements of 35 U.S.C. § 101 for utility, and the written description requirement cannot be used to contravene that finding.

With respect to the comments in the Office Action concerning the phrase "modulating apoptosis," it is understood that the same protein can either inhibit or stimulate apoptosis. For example, Bcl-B itself can be associated with either anti-apoptotic proteins such as Bcl-2 or Bcl-X_L or with pro-apoptotic proteins such as Bax (page 14, lines 15-16). Accordingly, the recitation of "modulating apoptosis" is appropriate as the activity of the protein in either stimulating or inhibiting apoptosis depends on the cellular context and the proteins with which Bcl-B interacts. Therefore, nucleic acids can encode proteins that may stimulate apoptosis in one context and yet

inhibit apoptosis in another context. This does not create any basis for a rejection under the first paragraph of 35 U.S.C. § 112.

In order to advance prosecution, Applicants have added new claims directed specifically to SEQ ID NO: 1. These claims are new claims 142-163. The addition of these claims is merely to advance prosecution and is not to be taken as an admission that any other claims fail to meet the written description requirements or the enablement requirements, to be discussed below.

The specification is sufficient to describe the invention "so that one skilled in the art can recognize what is claimed." Enzo Biochem, Inc. v. Gen-Probe, Inc., 62 U.S.P.Q. 2d 1289, 1293-94 (Fed. Cir. 2002) ("Enzo I"). That standard is clearly met here. Moreover, it is well-established that an applicant need not disclose every species encompassed by a claim. In re Angstadt, 190 U.S.P.Q. 214 (C.C.P.A. 1976).

Accordingly, this rejection is respectfully traversed as applied to the amended claims. The Examiner is therefore respectfully requested to withdraw the rejection.

B. The Rejections of Claims 1-10, 12-23, 26-28, 42-45, and 76-77 Under the First Paragraph of 35 U.S.C. § 112 for Failure to Comply with the Enablement Requirement

Claims 1-10, 12-23, 26-28, 42-45, and 76-77 were rejected under the first paragraph of 35 U.S.C. § 112 for lack of compliance with the enablement requirement.

As applied to the amended claims, this rejection is respectfully traversed.

It is established law with respect to enablement that the specification must be taken as being in compliance with the first paragraph of 35 U.S.C. § 112 unless there

is reason to doubt the objective role of the statements contained in the specification which must be relied upon for enabling support. In re Marzocchi, 169 U.S.P.Q. 367 (C.C.P.A. 1971). There has in fact been no suggestion that it would constitute undue experimentation to make or use any of the nucleotides within the scope of the claims. Methods for the preparation of nucleotide sequences, including PCR amplification and solid-phase polynucleotide synthesis, to name several techniques, are well understood in the art and there use to create any sequence within the scope of the claims would not constitute undue experimentation. Also, it is relatively simple for one of ordinary skill in the art to use appropriate software programs such as BLAST to provide a nucleotide-by-nucleotide comparison of sequences to determine whether they meet any specified level of identity. This also does not constitute undue experimentation.

Moreover, properly reasoned and supported statements explaining any failure to comply with the enablement requirements of 35 U.S.C. § 112 are a requirement to properly support such a rejection. The absence of such properly reasoned and supported statements compels withdrawal of this rejection. In re Wright, 27 U.S.P.Q. 2d 1510 (Fed. Cir. 1993). The Office Action merely states: "Without a clear disclosure of the sequences encompassed by the claims one of skill in the art would not know how to make or use the claimed invention without performing an undue amount of additional experimentation to first identify the sequences having the desired function." That statement does not provide "properly reasoned and supported statements" as to why enablement is not present. The question, from the standpoint of compliance with the enablement requirement of the first paragraph of 35 U.S.C. § 112, is whether the specification enables one of ordinary skill in the art to prepare and use the required nucleotide sequences. The answer, in view of the specification and examples, to this question is undoubtedly affirmative.

The specification need not recite details of the claimed invention where one of ordinary skill in the art would consider these details obvious or well known in the art. In re Skirvan, 427 F.2d 801, 166 U.S.P.Q. 85 (C.C.P.A. 1970). The quantity of

detail permitted to be omitted can be substantial when the state of the art is such that the detail could be readily supplied by one of ordinary skill in the art. This is true even if no working examples are furnished. In re Strahilevitz, 668 F.2d 1229, 212 U.S.P.Q. 561 (C.C.P.A. 1982) (immunochemistry).

Even should considerable experimentation be required, this does not constitute "undue experimentation" if the experimentation required is routine and the worker is given sufficient guidance. "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." In re Colianni, 195 U.S.P.Q. 150, 153 (C.C.P.A. 1977). Thus, the amount of experimentation that *might* be required does not give rise to a conclusion of lack of enablement. Moreover, complete reproducibility is not required to find enablement. Johns Hopkins University v. CellPro, Inc., 47 U.S.P.Q. 2d 1705 (Fed. Cir. 1998). In fact, under the holding of Johns Hopkins University, the fact that some attempts at reproducing the claimed invention fail does not lead to a conclusion of undue experimentation. In Johns Hopkins University, the invention concerned monoclonal antibodies, and attempts to reproduce the claimed invention did not uniformly result in success. The Federal Circuit held that this did not constitute undue experimentation, because a certain amount of experimentation was inherent in the Kohler-Milstein process for producing monoclonal antibodies, and a certain degree of irreproducibility was expected. Id.

The degree of unpredictability must be considered within the context of the invention and the knowledge of those skilled in the art. Even broad claims can be enabled if the subject matter of the claims is such that the unpredictability of what is actually claimed is minimized. See In re Vaeck, 20 U.S.P.Q. 2d 1438, 1444-45 (Fed. Cir. 1991) (claims directed to expression of chimeric genes in specific genera of cyanobacteria allowable even though claims were not limited to expression of genes encoding particular Bacillus proteins in view of extensive understanding in the prior art of toxicity of Bacillus proteins). The skill of those of ordinary skill in the art clearly encompasses the preparation and use of nucleotide sequences that possess a defined

degree of identity with SEQ ID NO:1. This is another strong argument for enablement of the claimed invention.

All that is required to provide enablement is that any mode of making and using the invention be recited in the specification. Engel Industries, Inc. v. Lockformer Corp., 946 F.2d 1528, 20 U.S.P.Q. 2d 1300 (Fed. Cir. 1991). This test is clearly met here by the specification in view of what is known in the art.

Moreover, there is no requirement that all compositions within the scope of the claimed methods provide the same degree of efficacy or activity. In re Gardner, 177 U.S.P.Q. 396 (C.C.P.A. 1973); In re Fouche, 169 U.S.P.Q. 429 (C.C.P.A. 1971). The fact that some of these nucleotide sequences may, for example, encode proteins that have a greater effect on apoptosis than others does not mean that undue experimentation exists.

As is frequently the case in enablement questions, a review of the factors set forth by the Federal Circuit in In re Wands, 858 F.2d 731, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988), is useful. The Wands factors are: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented: (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. Id.

A review of these factors indicates that enablement is present. The conclusion is that a rejection under the first paragraph of 35 U.S.C. § 112 should be withdrawn.

The quantity of experimentation required is not excessive in view of the subject matter. As indicated above, methods for the synthesis and comparison of nucleic acid sequences are well understood in the art. When these methods are combined with

the teachings of the specification, there is little experimentation to be carried out by one of ordinary skill in the art. What experimentation is required is routine in view of the well-understood nature of the methods.

The nature of the invention is such that undue experimentation is not present, when the scope of the claimed invention is taken into account. The claimed invention, from the standpoint of enablement, is of a relatively restricted scope as to what must be shown to constitute enablement. The activities of these nucleic acid sequences are not in question. These are not claims for which a degree of extrapolation is required such that the extrapolation would lead to a conclusion of undue experimentation based on the burden placed on one of ordinary skill in the art to achieve enablement within the scope of the claimed invention. Compare In re Strahilevitz, 668 F.2d 1229, 212 U.S.P.Q. 561 (C.C.P.A. 1982) (enablement found even though no working examples present) with In re Fisher, 427 F.2d 833, 166 U.S.P.Q. 18 (C.C.P.A. 1970) (no enablement for claims to an ACTH preparation having a potency of at least 1 international unit/mg, with no upper limit, when specification disclosed preparation of ACTH of potency between 1.11 and 2.30 international units/mg). Here, the scope of the protection sought is relatively circumscribed and the degree of experimentation required is minimal.

The state of the prior art does not suggest an exceptional degree of unpredictability with respect to the structure or function of these nucleotide sequences. As recited above, it is extremely easy for one of ordinary skill in the art to determine sequences that meet the criterion of a specified degree of identity to SEQ ID NO:1 and then to synthesize or replicate such sequences.

The relative skill of those in the art is high. This invention is directed to biochemists, microbiologists, and cell biologists, typically with a Ph.D. or other advanced degree in the relevant discipline.

The predictability or unpredictability of the art was discussed above. As indicated, the degree of unpredictability in the structure and function of these sequences is reduced by the availability of well-understood algorithms for determining the degree of identity between two nucleotide sequences and by the availability of well-understood tools for synthesis or replication of these sequences.

In fact, the Federal Circuit itself, in Wands, found that enablement existed and that undue experimentation was not present. It held that "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." In re Wands, 858 F.2d at 737, 8 U.S.P.Q. 2d at 1404. Wands involved monoclonal antibodies produced by hybridomas. The monoclonal antibodies had to have a certain degree of affinity toward their corresponding antigen. Of 143 hybridomas produced, only 9 were screened further, and of those 9, only four were found to fall within the scope of the claimed invention. This was sufficient to find enablement in the technology under consideration. The fact that some sequences within the claims may not have the desired function does not give rise to a finding of undue experimentation and thus lack of enablement under the first paragraph of 35 U.S.C. § 112. Atlas Powder Co. v. E.I DuPont de Nemours & Co., 224 U.S.P.Q. 409 (Fed. Cir. 1984).

As long as the specification discloses at least one method for making and using the claimed invention that bears a "reasonable correlation" to the entire scope of the claimed invention, the enablement requirement of the first paragraph of 35 U.S.C. § 112 is satisfied. In re Fisher, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). That test is met here in view of the teachings of the specification and the knowledge of those in the art.

The situation here is analogous to that in Wands. The claims are of such a scope that one of ordinary skill in the art could use the claimed invention with a

reasonable probability of success. That is all that is required for to meet the requirement for enablement under the first paragraph of 35 U.S.C. § 112.

Accordingly, the Examiner is respectfully requested to withdraw this rejection as applied to the amended claims.

IV. THE PRIOR ART REJECTIONS

Claims 1-3, 5-23, and 26-28 were rejected under 35 U.S.C. § 102(b) as anticipated by PCT Patent Publication No. WO 00/00506 by Kato et al. ("Kato et al. '506"). Applicants have amended the claims to recite that there is greater than 91.6% identity between the sequence recited in the claims and SEQ ID NO:1. This obviates any basis for rejection, for there is no teaching or suggestion in Kato et al. '506 of any sequence with a greater than 91.6% identity to the sequence of SEQ ID NO:1. There would also be no reason to modify the sequence of Kato et al. '506 so that a sequence with greater than 91.6% identity would result. This is true even though the sequence of Kato et al. '506 can be incorporated in an expression vector, the expression construct can include a promoter, and the construct can include a viral vector or can transform a cell. The requirement for the degree of identity recited in the claims is amended is not met. This obviates the basis for this rejection.

V. CONCLUSION

In conclusion, the claims remaining for consideration particularly point out and distinctly claim that which Applicants regard as their invention. These claims meet the written description and enablement requirements of the first paragraph of 35 U.S.C. § 112. They are free of the prior art, whether considered individually or in combination. Accordingly, allowance of these claims is respectfully requested.

If any issues remain, the Examiner is respectfully requested to telephone the undersigned at (858) 450-0099 x302.

Respectfully submitted,

Date: March 17, 2005

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